Meningococcal Infection (Invasive)

Report Immediately by Phone

Also known as: Spinal or bacterial Meningitis, Meningococcemia

Responsibilities:

Hospital/Infection Preventionist: Report by phone immediately

Lab: Report by phone immediately; send all isolates from invasive sites to SHL for testing and

serogrouping

Physician: Report by phone immediately

Local Public Health Agency (LPHA): Follow-up required

Iowa Department of Public Health

Disease Reporting Hotline: (800) 362-2736

Secure Fax: (515) 281-5698

1) THE DISEASE AND ITS EPIDEMIOLOGY

A. Agent

Invasive meningococcal infections are caused by the bacterium *Neisseria meningitidis* (meningococcus), a gram-negative diplococcus. There are 13 serogroups of *N. meningitidis*; nine of these serogroups are known to cause invasive disease (A, B, C1+, C1-, L, X, Y, W-135, and Z) in humans.

Note: Other organisms, including several viruses, can cause meningitis. This chapter is only referring to meningitis caused by *N. meningitidis*.

B. Clinical Description

Symptoms

Invasive infection with *N. meningitidis* may cause several clinical syndromes, including meningitis, bacteremia, sepsis or pneumonia. Symptoms of **meningitis** (infection of the meninges, the membrane covering the brain and spinal cord) typically include the sudden onset of a stiff neck, high fever and headache. A petechial rash (small red pinpoints that do not blanch when compressed) may also be present. Nausea, vomiting and mental confusion are often also present. **Meningococcemia** (infection of the blood) typically presents with the abrupt onset of fever, chills, malaise, prostration and rash (urticarial, maculopapular, purpuric or petechial).

Onset is usually abrupt.

Complications

Fulminant cases who present with purpura (large areas of subdermal bleeds), disseminated intravascular coagulation, shock, and/or coma and may lead to death within hours, despite appropriate therapy. The case-fatality rate for meningococcal meningitis and meningococcemia is about 5%-15%, even with appropriate antibiotic treatment. Persons with certain complement deficiencies (blood disorders that cause immunosuppression) are more susceptible, as are persons without a spleen or a functioning spleen.

C. Reservoirs

Humans are the only known reservoir of *N. meningitidis*. Approximately 5 to 10% of the population may carry this bacteria in the nasopharynx at any given time.

D. Modes of Transmission

The principal mode of transmission of *N. meningitidis* is person-to-person through direct contact with a case's oral or nasal secretions. The bacteria may also be spread through droplets or via an inanimate vehicle contaminated with saliva (*e.g.*, a cigarette, baby's toy or water bottle).

E. Incubation period

The incubation period ranges from 2-10 days, with an average incubation period of 3-4 days. Due to the asymptomatic carrier state, it is usually difficult to determine when exposure occurs.

F. Period of Communicability or Infectious period

Cases remain infectious as long as meningococci are present in oral secretions or until 24 hours after initiation of treatment with the appropriate antibiotic. Most carriers do not easily spread the organism.

G. Epidemiology

Sporadic cases and occasional outbreaks of invasive meningococcal disease occur worldwide. A "meningitis belt" extends from sub-Saharan Africa into India/Nepal, and invasive meningococcal disease due to *N. meningitidis* serogroup A is considered endemic in these areas. Epidemics of meningococcal meningitis also occur in this meningitis belt every 8 - 12 years and last from 2 - 4 years. Seasonal variations occur in these epidemics. Highest rates usually occur in dry, hot seasons, (December through June). The prevalent serotypes of *N. meningitidis* in other parts of the world may vary over time and by geography.

In the United States, the largest number of cases of invasive meningococcal disease usually occurs during the winter and early spring, coincident with an increase in the occurrence of acute respiratory infections. Historically in the U.S., cases of invasive meningococcal disease were most commonly seen in children <11 years old. Sporadic cases of meningococcal disease account for more than 98% of cases. Meningococcal pneumonia is more commonly seen in older patients. In the U.S., outbreaks of invasive meningococcal disease occur most frequently in crowded conditions (i.e., military bases, college dormitories). Cases of invasive meningococcal disease in the U.S. are most often caused by serogroups B, C and Y (each accounting for approximately 30% of reported cases), although other serogroups are also seen sporadically. Epidemics of invasive disease are most commonly associated with serogroups C and Y. Serogroup A is seen rarely in the U.S.

Since the 1990s, meningococcal diseases has been declining in the US, with 550 cases reported in 2013. In 2011, Iowa reported 12 cases; 6 were group B, 4 were group Y, 2 were group W-135, and 2 were undetermined, whereas in 2013 only one case was reported, and it was serogroup C.

Meningococcal carriage: *N. meningitidis* typically colonizes the nose and throat of 5-10% of the general population at any given time. These carriers are generally asymptomatic, and carriage of the bacteria may act as an immunizing exposure. By young adulthood, the majority of people in the United States have measurable antibody to the pathogenic serogroups of *N. meningitidis*. Carriers can spread the bacteria to others through saliva and respiratory secretions. Factors that increase colonization are antecedent upper respiratory tract infection, household crowding and both active and passive smoking.

H. Bioterrorism Potential

None.

2) DISEASE REPORTING AND CASE INVESTIGATION

A. Purpose of Surveillance and Reporting

• To identify close contacts of the case and provide recommendations for appropriate preventive measures and thus prevent further spread of infection.

- To provide information about the disease, its transmission, and methods of prevention.
- To promptly identify clusters or outbreaks of disease and initiate appropriate prevention and control measures.

B. Laboratory and Healthcare Provider Reporting Requirements

Iowa Administrative Code 641-1.3(139) stipulates that the laboratory and the healthcare provider immediately report any suspected or confirmed case. The disease reporting number for the Center for Acute Disease Epidemiology (CADE) is (800) 362-2736. After business hours, call the Iowa State Patrol Office at (515) 323-4360 and they will page a member of the on-call CADE staff.

Laboratory Testing Services Available

The University of Iowa State Hygienic Laboratory (SHL) will confirm and serogroup isolates of *N. meningitidis*. Laboratories are required to submit all isolates cultured from normally sterile sites for serogrouping. This serogrouping aids in public health surveillance and prevention of transmission. In addition, SHL will isolate the organism from appropriate clinical samples upon request. For more information on submitting specimens, contact SHL at (319) 335-4500, or visit: www.shl.uiowa.edu/

Note: Isolates obtained from sputum or throat cultures are not considered to come from sterile sites; therefore *N. meningitidis* from these sites is in itself not indicative of invasive disease and is not reportable. If a patient with culture-positive sputum has an illness compatible with invasive meningococcal disease, this should be reported and the appropriate sterile sites should then be cultured.

C. Local Public Health Agency Follow-up Responsibilities

Case Investigation

- a. Report suspect or confirmed cases of meningococcal disease **immediately** to CADE by calling (800) 362-2736. This disease requires immediate follow-up with prophylaxis given to contacts of the case.
- b. After notification of CADE, it is the LPHA, along with the hospital infection preventionist's, responsibility to investigate by asking the questions on and complete an Invasive Meningococcal Disease case investigation by interviewing the case and/or others who may be able to provide pertinent information. CADE staff is available 24/7 to assist in the follow-up of a case. The preferred method of case investigation is by using the Iowa Disease Surveillance System (IDSS).
- c. The main focus when following up a case of invasive meningococcal disease is to prevent additional cases of disease in contacts of the case. The investigation form will assist in collecting the appropriate information for complete contact identification and referral.
- d. The first step to following up a case of invasive meningococcal infection is to confirm the diagnosis. Often, reported cases of "meningitis" are ultimately found to be caused by bacteria other than *Neisseria meningitidis* or by a virus. Ask for antigen testing if antibiotics were started before cultures were taken. When *N. meningitidis* is suspected or confirmed, public health actions need to be taken quickly to protect contacts.
- e. Use the following guidelines to assist in completing the Meningococcal Disease Case Investigation.
 - 1) Record the demographic information, collecting as much case information as possible, including address, place of work, occupation, and child care or school information.
 - 2) If the case is hospitalized, collect hospital and transfer hospital information, if applicable. Hospital laboratories, direct caregivers and infection prevention practitioners are key in obtaining information for confirming a diagnosis.
 - 3) Collect clinical information on the case including laboratory data, clinical manifestations, and onset date information. This information is best collected from the infection prevention practitioner at the hospital or the case's healthcare provider.

- 4) Collect as much information as possible about the case's activities and contacts during the 7 days prior to the onset of illness. This information may be obtained from the case, the case's family and friends, school or child care personnel, or others involved with the case. Those who meet the definition of a close contact (see Section 4B below) of a case of invasive meningococcal disease must be educated on risk of disease and the importance of receiving prophylaxis. They should immediately be referred to their healthcare provider for appropriate post-exposure antibiotic therapy. Sample letters for notifying contacts in a school, child care or office are at the end of this chapter.
- f. Use the following guidelines to assist you in completing the Meningococcal Disease case investigation and entering the information into the Iowa Disease Surveillance System (IDSS)
 - 1) Specify the type of infection caused by *N. meningitidis*.
 - 2) Indicate the type of specimen from which *N. meningitidis* was isolated/identified.
 - 3) List the laboratory tests performed. For example, *N. meningitidis* was culture-confirmed or identified by bacterial antigen screen. Also include the date the specimen was drawn for the first positive culture.
 - 4) If known, provide the serogroup and antibiotic resistance information.
 - 5) If the case attends child care or school, list the child care/school name and provide a contact name and phone number.
 - 6) If the case attends college, indicate the name of the college, the case's year in school, and the case's living situation.
 - 7) If the case has received meningococcal vaccine, record the type of vaccine used, date administered, and reason for administration.
 - 8) If several attempts have been made to obtain case information, but have been unsuccessful (e.g., the case or healthcare provider does not return calls or respond to a letter, or the case refuses to divulge information or is too ill to be interviewed), call CADE and then enter as much information as is possible. Note in IDSS the reason why specific information could not be entered. Contact CADE immediately if key information is difficult to obtain.
- g. After completing the Meningococcal Disease case investigation, enter information into IDSS or fax to (515) 281-5698.
- h. Institution of disease control measures is an integral part of case investigation. It is the LPHA responsibility to understand and institute the control guidelines listed below in Section 4).

4) CONTROLLING FURTHER SPREAD

A. Isolation and Quarantine Requirements

Minimum Period of Isolation of Patient

Until 24 hours after the initiation of appropriate antibiotic therapy.

Minimum Period of Quarantine of Contacts

None.

B. Chemoprophylaxis is recommended for the following:

Case:

If neither a third generation cephlosporin nor ciprofloxacin was given as treatment, patients with meningococcal invasive disease should receive antibiotic prophylaxis prior to discharge to ensure elimination of nasopharyngeal carriage.

Contacts:

Because the rate of secondary disease for close contacts is highest immediately after onset of disease in the index patient, antimicrobial chemoprophylaxis should be administered as soon as possible

(ideally <24 hours after identification of the index patient). Conversely, chemoprophylaxis administered >14 days after onset of illness in the index patient is probably of limited or no value. Chemoprophylaxis is indicated for persons who in the 7 days before onset of illness or until 24 hours after the case had begun an effective antibiotic had close contact with the case. The definition of close contact is not precise but is intended to include to include persons who have had prolonged (8 hours or more) contact while in close proximity (3 feet is the general limit for large-droplet spread) to the case who have been directly exposed to the cases oral secretions. Close contact examples include:

- Household contact,
- Child care contact,
- Direct saliva contact with the case through kissing or sharing items like toothbrushes, water bottles or eating utensils,
- Mouth to mouth resuscitation or unprotected contact during endotracheal intubation,
- Frequently slept or ate in the same dwelling,
- Passengers seated directly next to the index case during airline flights lasting more than 8 hours, and
- Laboratory workers
 - All laboratory work with cultures of known or suspect *N. meningitidis* must be performed inside a biological safety cabinet. If a laboratory worker has been exposed via manipulating a known *N. meningitidis* culture outside of a biological safety cabinet, prophylactic antibiotic treatment is recommended to reduce the risk of infection and colonization.

Contacts who have previously received meningococcal vaccination should still receive chemoprophylaxis. Contacts should receive chemoprophylaxis as soon as possible, preferably within 24 hours after the index case has been identified, though diminishing levels of benefit may still be realized even with delays of up to 2 weeks.

Close contact does not include casual contacts at work or school or hospital employees who give routine care, even with 8 hours of contact within the previous week

Contacts of the case should be identified and referred to their healthcare provider for antibiotic prophylaxis.

Any contact that develops symptoms suggestive of meningococcal disease within 3-4 weeks after exposure should be evaluated promptly by a physician.

Recommendations for chemoprophylaxis are based on the assumption that persons of any age may be susceptible to meningococcal infections. Refer to table 2-4. Routine throat or nasopharyngeal culture of contacts is not helpful in determining who warrants chemoprophylaxis and unnecessarily delays the process.

Table 2-4. Chemoprophylaxis of Contacts to Meningococcal Disease

Drug Dosage		
Rifampin*	Children <1 month	5 mg/kg BID x 2 days
	Children ≥1 month	10 mg/kg (maximum single dose 600 mg) BID x 2 days
	Adults	600 mg BID x 2 days
Ceftriaxone	Children <15 years	125 mg IM (single dose)
	Adults, teenagers ≥15	250 mg IM (single dose)
Ciprofloxacin**	Nonpregnant adults (≥18 years of age)	500 mg PO (single dose)

BID = twice daily

Note on Rifampin:

Resource available at end of chapter - *Neisseria Meningitidis* Invasive Disease Chemoprophylaxis Algorithm

Rifampin Preparations for Administration (Meningococcal disease)

Persons taking rifampin should be informed that orange discoloration of urine, discoloration of soft contact lenses, and decreased effectiveness of oral contraceptives could occur.

Rifampin prophylaxis is best administered through the private physician and local pharmacy. However occasionally help must be given, i.e., contact has no doctor, pharmacy closed or has no rifampin. In these cases, call CADE. Dosages are calculated on weight and a prescription label with directions should accompany any rifampin dispensed.

There are two satisfactory procedures for the administration of rifampin to young children.

- 1. Rifampin Suspension may be available at the local pharmacy. When stored in the refrigerator, this suspension is stable for six weeks. In order to assure a uniform dosage, it is extremely important to shake the suspension vigorously just before the administration of each dose to the patient.
- 2. Applesauce Mix*
- Empty the contents of one rifampin 300 mg capsule in six teaspoons of applesauce and mix thoroughly (preparation contains 50 mg/5 ml or per teaspoon).
- Dosage must be calculated and family counseled on number of teaspoons to administer.
- Unused applesauce mixed with rifampin should be immediately discarded. New applesauce-rifampin mix should be made for each dose.
- *Preparation of Choice

Note: Rifampin administration has not been approved in any other preparation or solution. If the contact's healthcare provider is not available, contact the local board of health physician or CADE for assistance.

^{*}Rifampin is not recommended for pregnant women who are contacts of cases because the effect of Rifampin on the fetus has not been established. If contact is pregnant have her contact her OB/GYN doctor immediately for consultation on appropriate antibiotic prophylaxis.

^{*}Side effects of Rifampin include: orange discoloration of urine, discoloration of soft contact lenses (removal recommended for duration of chemoprophylaxis), decreased effectiveness of oral contraceptives, discoloration of teeth, nausea, vomiting, and diarrhea. These are uncommon when giving only 4 doses for prophylaxis.

^{**}Ciprofloxacin is not usually recommended for persons younger than 18 years of age or for pregnant or lactating women, because studies in animals have shown it causes cartilage damage in immature animals. The drug can be used for chemoprophylaxis in children when no acceptable alternative is available. There have been no reports of irreversible adverse effects in cartilage or age-associated adverse events among children and adolescents.

C. Managing Special Situations Child Care

Please contact CADE (800) 362-2736 immediately to discuss.

A case of invasive meningococcal illness in a child care setting often causes panic among parents and the community. Although the risk of transmission in this setting remains relatively low, chemoprophylaxis for all the children in the child care class or the child care facility may be recommended because the physical interactions between young children often involve direct saliva contact.

Chemoprophylaxis is recommended for:

All children and employees in child care who have had direct saliva contact or have been in the same classroom with the case in the week before onset or until 24 hours after the case was started on an effective antibiotic.

Surveillance for additional cases of disease should also be heightened. Contact the CADE to report suspect or confirmed cases in a child care (or any other setting). An epidemiologist will assist to ensure contacts are identified and notified. In addition, surveillance for new cases of disease should continue at the facility for at least 2 incubation periods (20 days) after the onset of the first case. If multiple cases occur, contact CADE immediately and continue surveillance for 2 incubation periods after the onset of the last case.

Resources in this manual:

- Fact Sheet for Child Care Administrators
- Parent and Employee Advisory Letter, Meningococcal Disease in a Child Care Center (case reported within 14 days after case's last day in child care)
- Parent and Employee Advisory Letter, Meningococcal Disease in a Child Care Center (case reported more than 14 days after case's last day in child care)

School

A case of invasive meningococcal illness in a school often causes panic among parents and the community. Although the risk of transmission in a school remains relatively low, the age and activities of the case will determine the extent of chemoprophylaxis necessary. Because the physical interactions between children often involve direct saliva contact, chemoprophylaxis for all the children in the case's class may be recommended, e.g. mentally handicapped students or very young children. An elementary, high school, or college student usually has a more defined group of close contacts and chemoprophylaxis may be more targeted.

Careful assessment and identification of contacts is needed to define the scope of chemoprophylaxis recommended. An epidemiologist will work with the local health agency to ensure an assessment and identification of contacts is completed and those needing post exposure prophylaxis are notified. Surveillance for additional cases of disease should also be heightened. Contact CADE to report suspect or confirmed cases. In addition, surveillance for new cases of disease should continue at the school for at least 20 days after the onset of the case. If multiple cases occur, contact CADE immediately and continue surveillance for 2 incubation periods (20 days) after the onset of the last case.

Community Residential Program

If a case of meningococcal disease occurs in a residential program, close contacts of the case should be referred to their healthcare provider for chemoprophylaxis. The activity in the facility should be assessed to determine the level of interaction between residents. The facility may be considered a "household setting" and require chemoprophylaxis of all residents, or the chemoprophylaxis may be more targeted. Contact the CADE for assistance in following up a case of invasive meningococcal disease in residential programs. In addition, surveillance for new cases of disease in the facility should continue for at least 2 incubation periods (20 days) after the onset of the first case. If multiple

cases occur, contact CADE immediately and continue surveillance for 2 incubation periods after the onset of the last case.

Reported Incidence Is Higher than Usual/Outbreak Suspected

If the number of reported cases in a jurisdiction is higher than usual for the time of year, or if an outbreak is suspected, contact CADE immediately at (800) 362-2736. This situation may warrant an investigation of clustered cases to determine a course of action to prevent further cases. The IDPH can perform surveillance for clusters of illness that may cross several county lines and therefore be difficult to identify at a local level. To assist in outbreak identification, it is critical that all invasive site *Neisseria meningococcal* isolates are sent to State Hygienic Laboratory (SHL) for serogrouping.

D. Preventive Measures

Personal Preventive Measures/Education

To prevent additional cases:

- Refer close contacts to healthcare providers for appropriate chemoprophylaxis.
- Advise contacts of signs and symptoms of illness and refer them to their healthcare provider should they experience any symptoms compatible with invasive meningococcal disease.
- Provide contacts with a *Meningococcal Disease Fact Sheet*.

To avoid future exposures, advise individuals to:

- Practice good hygiene and handwashing technique.
- Avoid sharing food, beverages, cigarettes or eating utensils.
- Consider immunization in certain circumstances (see below).

Immunization

Several meningococcal polysaccharide vaccines protecting against four serogroups (A, C, Y, and W-135) of *N. meningitidis* are are available. All 11-12 years olds should be vaccinated with meningococcal conjugate vaccine (MCV4). A booster dose should be given at age 16 years. For adolescents who receive the first dose at age 13 through 15 years, a one-time booster dose should be administered, preferably at age 16 through 18 years, before the peak in increased risk. Adolescents who receive their first dose of MCV4 at or after age 16 years do not need a booster dose.

Certain countries have licensed meningococcal serogroup B vaccines, but as yet are not routinely available in the US.

The Advisory Committee on Immunization Practices (ACIP) recommends that a student entering college get a booster dose of vaccine if they received the vaccine more than 5 years before starting college or if they never received one.

The vaccine is also recommended for travelers to countries where meningitis is endemic, certain high-risk individuals (those with terminal complement component deficiencies and those with anatomic or functional asplenia), laboratory personnel who are exposed routinely to *N. meningitidis* in solution that may be aerosolized, college freshman living in dormitories, military recruits, and in the case of an outbreak of invasive disease.

Meningococcal conjugated vaccine (MCV4) is preferable to meningococcal polysaccharide vaccine (MPSV4) for vaccination of children aged 2-10 years who are at increased risk for meningococcal disease. These children include travelers to or residents of countries in which meningococcal disease is hyperendemic or epidemic, children who have terminal complement component deficiencies and children who have anatomic or functional asplenia. Additionally, MCV4 is preferred to MPSV4 for use among children aged 2-10 years for control of meningococcal disease outbreaks.

The ACIP recommends that healthcare providers of college students provide information to students and their parents about meningococcal disease and the benefits of vaccination. In particular, vaccination should be made easily available to freshman students, (especially those living in group

settings like dorms). Iowa law requires that colleges with on campus housing educate incoming students on the vaccine.

N. meningitidis is spread through direct contact with oral or nasal secretions of a carrier. A closed setting such as a college dormitory, combined with high-risk behaviors in college students (alcohol consumption, exposure to tobacco smoke, sharing food or beverages, activities involving the exchange of saliva, etc.), may cause some college students to be at greater risk for invasive infection. Healthcare providers should discuss these risk factors and the likelihood that their patients will be involved in high-risk behaviors when evaluating patients for the administration of meningococcal vaccine.

4) ADDITIONAL INFORMATION

The Council of State and Territorial Epidemiologists (CSTE) surveillance case definitions for Meningitis can be found at: www.cdc.gov/osels/ph-surveillance/nndss/phs/infdis.htm#top

CSTE case definitions should not affect the investigation or reporting of a case that fulfills the criteria in this chapter. (CSTE case definitions are used by the state health department and the CDC to maintain uniform standards for national reporting.)

Comment

• Positive antigen test results from urine or serum samples are unreliable for diagnosing meningococcal disease, but can be used to assist in diagnosis if a positive result is obtained.

References

American Academy of Pediatrics. *2015 Red Book: Report of the Committee on Infectious Diseases, 30th Edition*. Illinois, American Academy of Pediatrics, 2015.

Heymann, D.L., ed. *Control of Communicable Diseases Manual, 20th Edition.* Washington, DC, American Public Health Association, 2015.

CDC, Laboratory-Acquired Meningococcal Disease – United States, 2000, MMWR, February 22, 2002; 51:7

Gardner, P., Prevention of Meningococcal Disease, The New England Journal of Medicine, October 5, 2006

Raghuanthan, P. L., Bernhardt, S. A., Rosenstein, N. E., Opportunities for control of meningococcal disease in the United States. Annu. Rev. Med. 2004. 55:333–53

Sejvar, James J., et al., *Assessing the Risk of Laboratory-Acquired Meningococcal Disease*, Journal of Clinical Microbiology, September 2005 4811-4814

Additional Resources

CDC. *Epidemiology and Prevention of Vaccine-Preventable Diseases.* (The Pink Book), 12th ed. Washington DC: Public Health Foundation, April, 2011.

www.cdc.gov/vaccines/pubs/pinkbook/downloads/mening.pdf

National Foundation for Infectious Diseases, <u>The Changing Epidemiology of Meningococcal Disease</u> CDC. Meningitis vaccination website. <u>www.cdc.gov/vaccines/vpd-vac/mening/default.htm</u>

Neisseria meningitidis Invasive Disease Chemoprophylaxis

Prophylaxis	No Prophylaxis	
Household contacts	— Casual Contacts at work or	
— Direct Saliva Contact	school	
Child care attendees	Hospital employees who give	
Laboratory workers at risk	routine care	

Chemoprophylaxis is indicated for persons having household-like and or direct saliva contact with the case in the week before onset or until 24 hours after the case has begun an effective antibiotic. Chemoprophylaxis is also indicated for laboratory workers who have manipulated a known *N. menigitidis* culture outside of a biological safety cabinet.

Chemoprophylaxis should be initiated within 24 hours of case identification, but no later than 14 days after exposure.

Vaccine is used in outbreak situations, not for postexposure chemoprophylaxis Questions? Call 1.800.362.2736